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(54) Title: FEED BISCUIT INCLUDING FAT IMBIBING POLYMER

(57) Abstract

A biscuit delivery system for orally delivering fat imbibing polymers to the gastro–intestinal tract of an animal. The fat imbibing polymer adsorb dietary fat from the gastro–intestinal tract, thereby reducing fat absorption by the subject. The biscuit includes a solid binder material in which the fat imbibing polymer is dispersed. The biscuit may include additional ingredients including flavoring and fat soluble vitamins.

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# FEED BISCUIT INCLUDING FAT IMBIBING POLYMER

This application claims the benefit of U.S. Serial No. 60/134,339, filed May 14, 1999.

U.S. Patents 4,432,968 and 4,695,621 describe pharmacologically-acceptable fat imbibing polymers which can be orally administered to animals to control body weight. The fat imbibing polymers are indigestible and preferably granular or microsphere in shape (herein collectively referred to as "beads") and have a particle size or diameter of from 0.05 to 2000 microns. The polymer beads comprise crosslinked copolymers of an ethylenically unsaturated monomer, for example, isobornyl acrylate, isobornyl methacrylate, styrene, or alkylstyrene and an ester of a fatty alcohol. The fat imbibing polymer beads are orally administered as formulations in admixture with a pharmaceutically acceptable carrier. Preferred carriers include water or aqueous dilute ethanol, both of which can also include flavoring agents. The polymers can also be administered in the form of dosage units, each dosage unit comprising a pharmaceutically acceptable carrier and an effective dosage of the polymer sufficient to absorb a substantial amount of dietary fat normally consumed by the animal at a single feeding. Suitable suspending agents include: hydroxypropyl methylcellulose, carboxymethyl cellulose, pectin, tragacanth, and sodium stearate. Preferred dosage units are gelatin capsules containing solid particulate polymer and individual units of an aqueous suspension of the polymer containing a pharmaceutically-acceptable suspending agent.

These fat imbibing polymer beads typically have a detectable "gritty" texture. This texture is particularly noticeable when the beads are administered with a liquid delivery system. As a consequence of this undesirable texture, administration can be difficult as animals will often resist ingestion. Similarly, oral administration of the beads can be challenging with dosage units designed to be swallowed whole, such as gelatin capsules. For example, dogs and cats will often not voluntarily swallow such capsules. Attempts have also been made to intermix the beads with a subject's food. However, this approach is time consuming, messy and vulnerable to improper dosing. Moreover, although the beads can be administered concurrently with the subject's food, to be most effective the beads should be ingested prior to meal time, (for example, fifteen minutes to several hours before meal time depending upon the subject's size, weight and species). Furthermore, unlike powder or liquid form additives, the

subject beads can be quite dangerous if spilled on hard surfaces as the beads function as miniature ball bearings creating a very slick surface. Given their relative small size, proper clean up of spills can be time consuming.

Thus, a convenient delivery system for orally administering fat imbibing polymer beads is sought which addresses the aforementioned concerns.

The present invention is a biscuit for reducing dietary fat absorption in animals. The subject biscuits include a fat imbibing polymer capable of imbibing dietary fat from the gastro-intestinal tract of an animal. The polymer is preferably provided in a granular or microsphere form (hereinafter collectively referred to as "bead") which may be homogeneously distributed within a solid binder material. The solid binder disguises the gritty texture of the polymer beads making the ingestion the polymer beads more desirable. Moreover, unit dosing can be easily controlled on a per biscuit basis depending upon the subject's size and species. Furthermore, the biscuit vehicle provides a convenient pre-meal treat and avoids messy, time consuming preparation and administration. Finally, spillage of beads and clean up are avoided by binding the beads into a solid biscuit.

The term "biscuit" used herein describes a solid food product designed to be chewed ("masticated"), rather than swallowed whole. Although the size of the biscuit may vary depending upon the size and species of the subject, the biscuit should be of a size to contain an effective dosage of beads to adsorb an amount of dietary fat from a subsequent meal to provide the subject with a dietary benefit. For example, biscuits having a dimension of approximately: 2.5 cm x 1.3 cm x 0.6 cm may be suitable for small dogs, whereas biscuits for large dogs may be 10 cm x 2.5 cm x 1.3 cm

The subject biscuits include fat imbibing polymer beads, examples of which are described at in U.S. Patents 4,432,968 and 4,695,621. The specific quantity of beads included within a given biscuit will depend upon the size and species of the subject and the size of the biscuit.

The fat imbibing beads adsorb dietary fat from the gastro-intestinal tract of an animal. The term "dietary fat" is intended to include both solid and liquid materials generally comprising glycerol esters with higher fatty acids. Sources of dietary fat include both animal

(for example, bacon grease, butter, animal fat, lard, etc.) and plant (for example, corn oil, coconut oil, cottonseed oil, palm oil, etc.), including predominantly triglyceride esters of both saturated and unsaturated fatty acids as well as some free fatty acids. Glyceryl tristearate, glyceral tripalmitate and glyceryl trioleate are among the most common esters.

The subject biscuit includes a solid binder material for binding the beads and maintaining the shape of the biscuit. The binder material may include a variety of ingredients typically utilized in biscuit or cookie formulations. Applicable binder materials include flour, bran, rice, and/or corn meal based. Moreover, softening gums or cellulose thickeners may be utilized to modify the hardness of the biscuit. That is, soft chewy or hard crunchy biscuits can be made by proper selection of binder materials and other known additives. Low calorie or no-calorie biscuits may also be made by use of cellulose binders which are not digestible by the subject. An example of such a biscuit formulation is provided in U.S. Patent 4,892,748.

The subject beads are preferably distributed throughout the binder material in a relatively homogenous or random fashion.

Additional ingredients may also be included within the biscuit formulation including flavoring agents, nutritional supplements, for example, fat soluble vitamins, preservatives, and the like. Additional ingredients and biscuit formulations are provided in U.S. Patents 5,576,306; 5,721,221; and 5,789,393.

The indigestible, pharmacologically-acceptable, fat imbibing polymers employed in the invention are solid, particulate, including reticulate particles, lightly crosslinked copolymers of, for example, isobornyl acrylate, isobornyl methacrylate, styrene and/or alkylstyrenes (preferably tertiary-alkylstyrenes wherein the alkyl groups contain from 4 to 12 carbon atoms) and one or more alkyl esters of a $C_1$ to $C_{20}$ alcohol. The alkylstyrene can be, for example, 4-tert-butylstyrene, 4-tert-amylstyrene, 3,5-ditertbutylstyrene, 4-tert-hexylstyrene, 4-tert-octylstyrene or 4-tert-dodecylstyrene. Tertiary-butylstyrene (4-tertbutylstyrene "TBS") is a preferred alkylstyrene. The alkyl ester monomers can include, for example, butyl methacrylate, butyl acrylate, hexyl acrylate, 2-ethylhexyl acrylate, cetyl methacrylate, eicosyl acrylate, the mixed ester cetyl-eicosyl methacrylate, lauryl methacrylate, stearyl methacrylate or lauryl acrylate. The alcohol moiety of the ester is preferably of 8 to 20 carbon atoms, and is

preferably a linear fatty alcohol residue, such as cetyl, lauryl, stearyl or eicosyl, or a secondary alcohol residue.

The alkylstyrene is preferably the predominant monomer, making up at least 50 percent by weight, and preferably from about 60 to about 85 to 90 percent by weight of the total polymer. Isobornyl acrylate or isobornyl methacrylate can be substituted for the predominant alkylstyrene monomer. The alkyl ester monomer may include both a methacrylate ester and an acrylate ester of one or more $C_8$ to $C_{20}$ fatty alcohols.

The copolymer is preferably lightly crosslinked to insure that the polymer will not be soluble in or miscible with dietary fats and oils. Too much crosslinking, that is, 1.0 percent by weight or more, will hinder or prevent the polymer particles from imbibing fats. In general, the preferred polymers contain from about 0.001 to 0.3 percent, and more preferably 0.01 to about 0.1 percent by weight of a crosslinking agent (based on the total weight of the monomers). The crosslinking agent can be any di- or polyfunctional compound known to be useful as a crosslinking agent in polymeric vinyl addition compositions, such as divinylbenzene, vinyl isopropenyl benzene, or other polyethylenically unsaturated crosslinking agents described, for example, in U.S. Patent 3,520,806. Divinylbenzene is preferred as a crosslinking agent, in amounts from 0.025 to 0.075 weight percent.

The polymers are preferably, but not necessarily, prepared by emulsion or suspension polymerization of the monomers (and crosslinking agent) in an aqueous emulsion or aqueous suspension. In emulsion polymerization, the polymerization occurs in micelles formed by the monomer mixture and the emulsifier. In the suspension technique, polymerization occurs in monomer droplets suspended in the aqueous phase. Suspension polymerization is preferred for making larger particles, for example, from about 0.3 to 0.5 micron and larger.

The polymerization reaction proceeds at temperatures from about 50° to 120°C, conveniently from 70° to 90°C, and in the presence of a minor amount of polymerization initiator such as potassium persulfate or tertiary-butyl peroctoate. In preparing the copolymers, the monomers and crosslinking agent are mixed together, in the proportions corresponding to those desired for the product, then dispersed in water containing either an emulsifying agent or a suspending agent. The proportions are preferably selected so the

monomer plus crosslinking agent comprises about 20 to about 60 percent by weight of the aqueous mixture. The polymerization initiator is mixed with either the monomer mixture or the aqueous phase depending on the polymerization method, the initiator used and its relative solubility in the two phases. Optionally the monomer and aqueous phases can be mixed, for example, with a high-shear mixer or a homogenizer, to disperse the monomer phase in the aqueous phase, and to reduce the particle size monomer phase and to the size desired for suspension polymerization; and to form micelles of the desired size for emulsion polymerization. The resulting mixture is heated with stirring at a temperature in the polymerization temperature range until the reaction is substantially complete (generally 4 to 24 hours). The copolymer product can be recovered and worked up by conventional techniques such as filtration or screening to remove any coagulum or large-particle waste, dialysis, lyophilization or, particularly, with polymer particle sizes on the order of 0.15 micron and larger, by filtration to separate the reaction medium, alcohol precipitation, washing with lower alkanols, steam distillation of other known techniques.

In a convenient purification procedure for polymer particles prepared by suspension polymerization, the suspension is passed through a large screen to remove any large coagulum waste particles. Small suspension particles are allowed to settle, and the supernatant liquid removed by decantation. Large suspension particles can be separated by screens. The copolymer is preferably washed with water to remove residual suspending agent. The washed polymer particles can be separated by conventional techniques such as decantation, centrifugation, or filtration. The washed particles can be used directly, or suspended in an aqueous carrier.

Purification is preferably achieved by isolating the material as a filter cake and then sequentially washing the intact filter cake with deionized water and then an alcohol, such as food grade ethanol.

Examples

The following working example is given to illustrate the invention and should not be construed to limit its scope.

A fat imbibing polymer was prepared by suspension polymerization using a computer-automated 1-gallon stainless steel reactor that was jacketed for heating. The polymerization reactor was equipped with an agitator, a feed port, a drain valve, a vent valve, a nitrogen line, and a frangible.

Polymer beads were made by preparing an aqueous phase composed of 764 g of deionized water with 2.5 g of a 62 percent aqueous solution of sodium dichromate, 263 g of a 1 weight percent aqueous solution of carboxymethylmethyl cellulose (CMMC), and 2.1 g of a 1 weight percent aqueous solution of sodium lauryl sulfate. An organic phase was added consisting of 981 g of t-butylstyrene, 421 g of lauryl methacrylate, 1.27 g of divinylbenzene (55 percent purity), and 3.5 g of benzoyl peroxide. Once the constituents were combined, the reactor was stirred at 25°C for 60 minutes at 250 RPM to properly size the monomer droplets. The temperature was then ramped at 0.4°C/min to 72°C and held at temperature for 1080 minutes at 250 RPM. The reactor was than cooled to 25°C and the copolymer particles were removed, washed with ethanol and water, de-watered, air dried and screened. The average size (volume median diameter) of the polymer beads was 110 um.

The ability of the polymer to absorb a fatty compound was measured by placing 5.0 ml of the polymer and about 35 ml of Filippo Berio Extra Light olive oil in a NALGENE™ 35 ml Oak Ridge graduated centrifuge tube with a screw cap. The mixture was shaken at about 30 minutes intervals for the first 6 hours. After 6 hours the sample was centrifuged at 1000 rpm for 1 minute then the volume of the polymer beads was measured as 23.0 ml (360 percent increase). The mixture was shaken then allowed to sit for an additional 18 hours. The sample was centrifuged at 1000 rpm for 1 minute then the volume of the polymer beads was measured as 28.5 ml (470 percent increase).

Biscuits were prepared by mixing the following dry ingredients: 500 g of polymer, 231 g of all-purpose flour, 164 g of whole wheat flour, 103 g of rye flour, 214 g of bran, 42 g of non-fat dry milk and 13 g garlic powder. Yeast (9.0 g) was dissolved in 137 g of warm water then mixed with 555 g of tomato juice. The dry ingredients were mixed into the liquid using a Kitchen Aid five quart professional mixer, then kneaded for 3 minutes. The dough was weighed out into 10 g portions, rolled into a ball, then flattened onto a cookie baking sheet. The dough was baked for 1 hour at 330°F, then cooled in air overnight, and packaged in

plastic bags. Each biscuit weighed about 6.5 g and contained about 2.5 g of the subject polymer.

The biscuits were given to three dogs during a 14–18 week time period. Each dog was given the biscuits immediately before eating their normal food according to Table 1 provided below.

Table 1

| | Initial | Biscuits | Number | Final | Weight Loss | |
|---|---|---|---|---|---|---|
| Breed | Weight (lbs) | Per Day (#) | of Weeks (#) | Weight (lbs) | Total (lbs) | Per Week (%*) |
| Labrador Retriever | 112.5 | 9 | 14 | 107 | 5.5 | 0.35 |
| Golden Retriever | 105 | 8 | 18 | 97 | 8 | 0.42 |
| Beagle | 46 | 4 | 16 | 41 | 5 | 0.68 |

* Percentage loss of weight versus initial body weight

As indicated by the data provided in Table 1, all three dogs lost weight while they were given the biscuits containing the subject polymer. The dogs lost a total weight of 5–8 pounds - an average of about 0.5 percent of their initial body weight for each week during 14-18 week trial.

What Is Claimed Is:

1. A biscuit for reducing dietary fat absorption in animals comprising a solid binder material and fat imbibing polymer capable of imbibing dietary fat from the gastro-intestinal tract of an animal.

2. The biscuit of Claim 1 wherein the fat imbibing polymer is provided in a bead form which is homogeneously distributed within the solid binder material.

3. The biscuit of Claim 1 wherein the binder material comprises flour.

4. The biscuit of Claim 1 wherein the binder material comprises a non-digestible cellulose material.

5. The biscuit of Claim 1 further comprising fat soluble vitamins.

6. The biscuit of Claim 1 wherein the fat imbibing polymer comprises a crosslinked copolymer polymerized from a mixture comprising alkylstyrene monomers and alkyl ester monomers.

7. The biscuit of Claim 6 wherein the alkylstyrene monomers comprise t-butylstyrene.

8. The biscuit of Claim 6 wherein the alkyl ester monomers comprise 2-ethylhexyl acrylate.

9. The biscuit of Claim 6 wherein the alkyl ester monomers comprise lauryl methacrylate.

10. The biscuit of Claim 1 wherein the fat imbibing polymer comprises a crosslinked copolymer polymerized from a mixture comprising isobornylmethacrylate monomers and alkyl ester monomers.

# INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A23K1/16 A23K1/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A23K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, FSTA, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 4 223 023 A (FURDA IVAN)<br>16 September 1980 (1980-09-16)<br>column 1, line 12-29<br>column 2, line 23-35<br>claim 1; example 1 | 1-3 |
| Y | --- | 4-10 |
| Y | US 4 432 968 A (PAGE JUDITH L ET AL)<br>21 February 1984 (1984-02-21)<br>cited in the application<br>column 2, line 11-20<br>column 4, line 24-33<br>column 11, line 38-44<br>claims 1,19-37 | 4-10 |
| | ----- | |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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information on patent family members

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